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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/694,245	10/27/2003	Timothy A. Morris	1133.005US2	4050

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EXAMINER	
GRUN, JAMES LESLIE	
ART UNIT	PAPER NUMBER
1641	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/21/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/694,245	MORRIS, TIMOTHY A.	
	Examiner	Art Unit	
	James L. Grun	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 December 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-48* is/are pending in the application.

4a) Of the above claim(s) *41-48* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *27 October 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/27/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Applicant's election with traverse of Group I, claims 1-40, in the paper filed 06 December 2006 is acknowledged. The traversal is on the ground(s) that the claims of Groups I-III can be searched together. This is not found persuasive for the reasons of record because the explanations of different structures, modes of operation, functions, effects, scope, classifications, and fields of search, which are clearly not co-extensive, made in the restriction requirement of record are sufficient to provide a *prima facie* showing of a serious burden upon the examiner. The requirement is still deemed proper and is therefore made FINAL. Claims 41-48 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim.

The disclosure is objected to because of the following informalities: page 8, line 23, --Figures 1A-1B-- should be recited; page 8, line 23, "Panel A" should be deleted and --Fig. 1A-- inserted therefor; page 9, line 1, "Panel B" should be deleted and --Fig. 1B-- inserted therefor; page 45, line 7, it is believed that --glomerular-- was intended. Appropriate correction is required.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The specification is objected to under 35 U.S.C. § 112, first paragraph, as failing to provide an adequate written description of the invention, and failing to adequately teach how to make and/or use the invention, i.e. failing to provide an enabling disclosure.

Claims 1-37 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, and which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification, as originally filed, does not provide support for an antibody or other detection reagent having an IC_{50} for des-arginine fibrinopeptide B which differs from that for fibrinopeptide B "by less than 25%" as is now claimed. Applicant discloses that a single polyclonal antiserum comprising a single bleeding of a single rabbit (i.e. R4097, bleed I3) elicited by immunization with human fibrinopeptide B was selected as having the "best reactivity profile" for use and that this antiserum as a whole had a cross-reactivity with des-arginine fibrinopeptide B which was 75% of that with fibrinopeptide B as determined by IC_{50} values in a competitive enzyme-linked immunosorbent assay in which the competitive inhibition of the binding of the antibody to human fibrinopeptide B by the peptides was determined and related in a particular fashion (see e.g. pages 27-28 and 40-41). It is noted by the examiner that the result of 100% - 75% equals 25%, is not less than 25%, and even applicant's exemplified antibody therefore falls outside of the scope of the invention as is now claimed. The instantly claimed invention also does not set forth the relevant comparison for determining the difference in IC_{50} values and applicant's exemplified reagent falls further from the scope of the invention as is now claimed if the exemplified difference (2.2 nM) is related to the IC_{50} value for binding inhibition with fibrinopeptide B (6.7 nM), i.e. a difference of 33% (2.2 / 6.7 = .328). Although one of skill

in the art might realize from reading the disclosure that antibodies binding with nearly identical reactivity with des-arginine fibrinopeptide B and fibrinopeptide B are useable in the invention, such possibility of use does not provide explicit or implicit indication to one of skill in the art that an antibody or other detection reagent having an IC_{50} for des-arginine fibrinopeptide B which differs from that for fibrinopeptide B "by less than 25%" was originally contemplated as part of applicant's invention, particularly since applicant does not disclose or exemplify such a reactivity profile for the antibody, and such possibility of use does not satisfy the written description requirements of 35 U.S.C. § 112, first paragraph. Note that a description which renders obvious a claimed invention is not sufficient to satisfy the written description requirement. Applicant is requested to direct the Examiner's attention to specific passages where support for these newly recited limitations can be found in the specification as filed or is required to delete the new matter.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics when coupled with a known or disclosed structure/function correlation, methods of making the claimed product, or any combination thereof. The specification does not provide sufficient recitation of distinguishing identifying characteristics of the genus of "agents" other than for antibody populations or fragments thereof specific for the peptides (see e.g. page 6). *Vas-Cath Inc. v. Mahurkar*, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of

the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of agents and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016. The examiner would note that applicant also does not provide adequate written description of a single isolated antibody or fragment thereof having the properties of the exemplified polyclonal antibody population or the properties of the agent as are now claimed. Adequate written description requires more than a mere statement that a product is part of the invention and a reference to a potential method of isolating it. The product itself is required. Furthermore, In *The Reagents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of products by only their functional activity does not provide an adequate written description of the genus.

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115). However, the reproducibility of an antiserum with properties as claimed would seem unknown and unpredictable in view of the disclosure that only a single bleeding from a single immunized rabbit, selected as best for use, had properties close to those as claimed. Absent further written

description and guidance, one would have no assurance of predictably obtaining additional polyclonal antibody populations with the relevant properties for use.

In view of the lack of adequate written description of a single isolated antibody or fragment thereof having even the properties of the polyclonal antibody population noted above, one would therefore also have no assurance of the predictable ability to obtain and use an isolated or monoclonal antibody, or fragment thereof, with the properties as are now claimed. Moreover, in view of the guidance in the instant specification to no functional isolated species, the amount of experimentation required to determine functional structures, modifications, or properties for any usable species would be undue. Again, note that even an enabling disclosure for the preparation and use of only a few analogs of a product does not enable all possible analogs where the characteristics of the analogs are unpredictable. See *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.* (18 USPQ 2d 1027 (CAFC 1991)).

A patent is granted for a completed invention, not the general suggestion of an idea and how that idea might be developed into the claimed invention. In the decision of *Genentech Inc. v. Novo Nordisk*, 42 USPQ 2d 1001 (CAFC 1997), the court held that: "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable" and that "[t]ossing out the mere germ of an idea does not constitute enabling disclosure." The court further stated that: "when there is no disclosure of any specific starting material or of any of the conditions under which a process is to be carried out, undue experimentation is required; there is a failure to meet the enablement requirements that cannot be rectified by asserting that all the disclosure related to the process is within the skill

of the art", "[i]t is the specification, not the knowledge of one skilled in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement."

Claims 7, 9-10, 27, 31, 33, 36, and 39 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, and which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. The specification does not reasonably provide description of or enablement for any cell line producing a monoclonal antibody as instantly claimed.

Applicant provides guidance only for a potential method of making hybridomas which make monoclonal antibodies and provides no guidance as to what modifications or structure are important for the predictable function of any monoclonal antibody produced by any cell line. Very different structures may be found on antibodies with the same specificity. For example, very different variable heavy (V_H) chains can combine with the same variable light (V_L) chain to produce antibody binding sites with nearly the same size, shape, antigen specificity, and affinity. A similar phenomenon can also occur when different V_H sequences combine with different V_L sequences to produce antibodies with very similar properties. These observations indicate that divergent variable region sequences, both in and out of complementarity-determining regions, can be folded to form similar binding site contours, which result in similar immunochemical characteristics. Conversely, similar structure may be found on antibodies having different

specificities. In the absence of any guidance, one would not know or be able to predict or envision what structure or modifications were important for function of a monoclonal antibody in the invention and one could not envision properties of a functional hybridoma making same. Therefore, conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that a product is part of the invention and a reference to a potential method of isolating it. The product itself is required. Furthermore, In *The Reagents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of products by only their functional activity does not provide an adequate written description of the genus. The court indicated that although applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of products falling within the scope of the claimed genus. Applicant is reminded that the written description provision of 35 USC 112 is severable from its enablement provision. However, in view of the guidance in the instant specification to no functional species, the amount of experimentation required to determine functional structures, modifications, or properties for any usable species would be undue. For example, as noted above, very different structures may be found on antibodies with the same specificity, and conversely, similar structure may be found on antibodies having different specificities and one would not know, given the instant lack of written description and guidance and absent further unguided experimentation, what would predictably function in the invention. Note that even an enabling disclosure for the preparation and use of only a few analogs of a product does not enable all

possible analogs where the characteristics of the analogs are unpredictable. See *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.* (18 USPQ 2d 1027 (CAFC 1991)).

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-10, 21, and 35-40 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claims 1-10 and 35-40 it is not clear if applicant intends "defined by" as open or closed claim language.

In claims 1-8, improper Markush language is used to claim the members of the group. The alternatives "sequences...or" or "selected from...or" or "selected from the group consisting of...and" are acceptable.

In claims 9 and 10, improper Markush language is used to claim the members of the group. The alternatives "sequences...or" or "selected from...or" or "selected from the group consisting of...and" are acceptable.

Claim 21 might better depend from claim 27 or 28 to provide for an agent having the relevant structure to provide the relevant fragments.

In claims 35-37, improper Markush language is used to claim the members of the group. The alternatives "sequences...or" or "selected from...or" or "selected from the group consisting of...and" are acceptable.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in-
(1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or
(2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent,
except that an international application filed under the treaty defined in section 351(a) shall have the effects for the purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language;

Claims 1-7, 9-15, 21-27, 35, and 36 are rejected under 35 U.S.C. § 102(e)(2) as being clearly anticipated by Kudryk et al. (US 5,876,947).

Claims 38 and 39 are rejected under 35 U.S.C. § 102(e)(2) as being anticipated by Kudryk et al. (US 5,876,947).

Kudryk et al. (US '947) disclose monospecific antibodies which bind to an epitope as present in fibrinogen, fibrinopeptide B, or des-Arg fibrinopeptide B (SEQ ID NO:1), contained in its entirety by all of the instantly claimed sequences SEQ ID NOs:1-6, without regard to whether the C-terminal Arg residue has been cleaved from the fibrinopeptide B or whether the N-terminal residue is glutamine or pyroglutamic acid, and which is specifically exemplified by that monoclonal antibody produced by the P10 hybridoma, deposited as ATCC Accession No. HB-12398 (e.g. cols. 3-6, 7, 23). Antigen binding fragments Fab, $F(ab')_2$, or Fv of the monospecific antibodies, including that produced by the P10 hybridoma, are also disclosed. The antibody or fragment can be attached to a substrate or detectably labeled by conjugation to a

detectable moiety (see e.g. cols. 4, 11-12) for use in immunoassay detection of antigen and diagnosis of the presence or probability of thrombogenesis or atherogenesis in a subject (see e.g. cols. 3-6, 13, 15, 22). Antibodies can be elicited by conjugating a peptide via a Cys residue to a carrier such as keyhole limpet hemocyanin (e.g. col. 9). The antibodies can be provided in kits (see e.g. col. 16).

Claims 1-7, 9-15, 21-27, 35, and 36 are rejected under 35 U.S.C. § 102(a) as being clearly anticipated by Kudryk et al. (WO 99/05176).

Claims 38 and 39 are rejected under 35 U.S.C. § 102(a) as being anticipated by Kudryk et al. (WO 99/05176).

Kudryk et al. (WO '176) disclose monospecific antibodies which bind to an epitope as present in fibrinogen, fibrinopeptide B, or des-Arg fibrinopeptide B (SEQ ID NO:1) without regard to whether the C-terminal Arg residue has been cleaved from the fibrinopeptide B or whether the N-terminal residue is glutamine or pyroglutamic acid, and which is specifically exemplified by that monoclonal antibody produced by the P10 hybridoma (e.g. pages 5-6, 10, 12). Antigen binding fragments Fab, $F(ab')_2$, or Fv of the monospecific antibodies, including that produced by the P10 hybridoma, are also disclosed. The antibody or fragment can be attached to a substrate or detectably labeled by conjugation to a detectable moiety (see e.g. page 5) for use in immunoassay detection of antigen and diagnosis of the presence or probability of thrombogenesis or atherogenesis in a subject (see e.g. pages 6-8, 22, 31-32). Antibodies can be elicited by conjugating a peptide via a Cys residue to a carrier such as keyhole limpet hemocyanin (e.g. page 13). The antibodies can be provided in kits (see e.g. page 23).

Claims 38 and 40 are rejected under 35 U.S.C. § 102(b) as being anticipated by Qureshi et al. (Thromb. Haemostasis 42:1316, 1979) in light of Eckhardt et al. (J. Clin. Invest. 67:809, 1981), Bilezikian et al. (J. Clin. Invest. 56:438, 1975), and Wilner et al. (Biochemistry 18:5078, 1979).

Qureshi et al. predicted the clinical application of determinations of plasma fibrinopeptide B determinations by determination of the peptide in urine with the R29 and R30 antisera, having the properties as instantly claimed, in light of Eckhardt et al., Bilezikian et al., and Wilner et al., of binding to the peptides as instantly claimed wherein the $B\beta_{14}$ arginine residue is not critical for binding of the assayed fibrinopeptide antigen. The reagents of the reference appear to anticipate the "kit" of the instant claims.

Eckhardt et al., inter alia, teach radioimmunoassay for desarginine fibrinopeptide B in biological fluid samples using antibodies selected for reactivity for this antigen. The reference suggests the determination of fibrinopeptide B as an indicator of fibrin II formation and that the formation of fibrin II determines the occurrence of thrombosis (page 809, col. 2). The method of eliciting the antibodies of Eckhardt et al. with peptide conjugated to carrier protein, and the steps of the radioimmunoassay of Eckhardt et al. are taught in Bilezikian et al. The antisera used in Eckhardt et al., elicited by immunization with fibrinopeptide B conjugates (in light of Bilezikian et al.), which contain antibodies which bind to peptide epitopes as instantly claimed (see e.g. Table II, especially R29 and R30), are disclosed in Wilner et al.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
> (c) Subject matter developed by another person, which qualifies as prior art only under one or more subsections (e), (f) and (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

Claims 1-17 and 21-40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kudryk et al. (US 5,876,947), in view of Eckhardt et al. (J. Clin. Invest. 67:809, 1981).

Claims 1-17 and 21-40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kudryk et al. (WO 99/05176), in view of Eckhardt et al. (J. Clin. Invest. 67:809, 1981).

In contrast to the invention as instantly claimed, Kudryk et al. (US '947) or Kudryk et al. (WO '176) do not specifically teach oligoclonal antibodies for use in their methods, multiple determinations of fibrinopeptide levels in the same patient, or threshold levels as instantly claimed.

Eckhardt et al., inter alia, teach radioimmunoassay for desarginine fibrinopeptide B in biological fluid samples using oligoclonal antibodies selected for reactivity for this antigen. The reference suggests the determination of fibrinopeptide B as an indicator of fibrin II formation and that the formation of fibrin II determines the occurrence of thrombosis (page 809, col. 2). Multiple determinations of levels in the same patient over time to monitor the course of fibrinogenolysis treatment effects are taught.

It would have been obvious to one of ordinary skill in the art at the time the instant invention was made to have substituted oligoclonal antibodies in the methods of Kudryk et al. (US '947) or Kudryk et al. (WO '176) in view of the direct suggestion in the reference of Eckhardt et al. to perform the similar assay with oligoclonal antibodies. Determinations of threshold values indicative of disease would have been obvious to one of ordinary skill in the art since it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. *In re Aller*, 105 USPQ 233. It would have been further obvious to one of ordinary skill in the art at the time the instant invention was made to have performed multiple determinations on a patient with the methods of Kudryk et al. (US '947) or Kudryk et al. (WO '176), as modified, to determine the effects of treatments affecting fibrinogenolysis in view of the teachings of Eckhardt et al. regarding the detectable changes in plasma sample concentrations of fibrinopeptide B after such treatments.

Thus, the claimed invention as a whole was clearly prima facie obvious, especially in the absence of evidence to the contrary.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 38-40 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-23 of U.S. Patent No. 6,673,561, if necessary, in view of Kudryk et al. (US 5,876,947 or WO 99/05176). Although the conflicting claims are not identical, they are not patentably distinct from each other because the methods of the patent make obvious the kit of the instant application because it would have been obvious to have supplied the reagents required to perform the assay in a kit because that is conventional in the art for reproducibility, convenience, and economy, if necessary, as suggested in Kudryk et al. Moreover, the sequences as recited in the instant application are obvious in view of the known sequences of fibrinopeptide B and des-arginine fibrinopeptide B, if necessary as taught in Kudryk et al.

Claims 1-14 and 18-37 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-23 of U.S. Patent No. 6,673,561, in view of Kudryk et al. (US 5,876,947 or WO 99/05176). Although the conflicting claims are not identical, they are not patentably distinct from each other because the generic methods of the patent make obvious the instant specific claims in view of the specificity of the antibodies of Kudryk et al. (US 5,876,947 or WO 99/05176) as set forth previously in this Office action and incorporated herein.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Urano et al. (Thrombosis Res. 39:145, 1985) teach the relative concentrations of Bβ peptides detectable in plasma and urine samples from patients and that the concentrations increased and decreased in comparable fashion over the same time course after treatment (see e.g. Figs. 6 and 7).

Owens et al. teach antibody engineering for a variety of reasons, including the low cost of producing antibody derivatives in microbial systems.

Either of Bini et al. (Blood 69:1038, 1987) or Bini et al. (Arteriosclerosis 9:109, 1989) teach identification of fibrin(ogen) in normal samples and in thrombi and atherosclerotic lesions. However, the references do not teach the use of antibodies with the specificity as instantly claimed.

Kinjoh et al. teach a monoclonal antibody which binds to rabbit fibrinopeptide B and intact fibrinogen.

Burrows et al. teach determination of fibrinopeptide B for thrombosis detection. The date of publication/presentation is not clear but is asserted to be in 1999.

Campbell (1991) teaches the general procedure for the production of monoclonal antibodies (pages 3-6), conventional immunoassay design using immobilized antibodies (pages 21-23), and that substituting a monoclonal antibody for a polyclonal antibody in an established immunoassay "is not novel and is obvious" (page 45).

Chung et al. (Biochemistry 22:3244, 1983) teach the amino acid and nucleic acid sequences of the β chain of human fibrinogen.

Harlow et al. (1998) teach that, once the amino acid and/or nucleic acid sequences of a protein are known, it is routine and conventional in the art to elicit antibodies to peptides and/or fusion proteins derived from the protein and/or to prepare a bank of site-specific monoclonal antibodies for use (pages 72-77). The reference teaches that the easiest strategy to manipulate coupling of a peptide to a carrier for immunization is by the addition of an extra amino acid at either terminus of the peptide (e.g. page 77).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James L. Grun, Ph.D., whose telephone number is (571) 272-0821. The examiner can normally be reached on weekdays from 9 a.m. to 5 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le, SPE, can be contacted at (571) 272-0823.

The phone number for official facsimile transmitted communications to TC 1600, Group 1640, is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application, or requests to supply missing elements from Office communications, should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

James L. Grun, Ph.D.
February 18, 2007

CHRISTOPHER L. CHIN
PRIMARY EXAMINER
GROUP ~~1800~~ 1641
2/18/07